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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/716,141	11/18/2003	Matthias Eckhardt	01-1419	7030

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EXAMINER	
BERCH, MARK L	

ART UNIT	PAPER NUMBER
1624	

MAIL DATE	DELIVERY MODE
04/21/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/716,141	ECKHARDT ET AL.	
	Examiner	Art Unit	
	/Mark L. Berch/	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8,10,12,14 and 16-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,8,10,12 and 16-20* is/are rejected.

7)☒ Claim(s) *4-6 and 14* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *02/20/2008; 03/27/2008* .
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 10, 19-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "arthritis" is indefinite. By itself, it is not a standard medical term for a specific disease or group of related diseases, but a general term denoting inflammation of the joints, and may or may not involve inflammation of other parts of the body such as the nails. It mostly commonly refers to any of osteoarthritis, gouty arthritis, or rheumatoid arthritis. These are three totally different and unrelated disorders, which all have "arthritis" in their name and involve inflammation of the joints. Rheumatoid arthritis is an inflammatory disorder causing destruction of articular cartilage. It is an autoimmune condition where the body's immune system attacks its joints. It is a multisystemic disease, having extra-articular manifestations (e.g anemia, Keratoconjunctivitis sicca, lung fibrosis) which distinguish this disease from osteoarthritis (hence it is). In gouty arthritis, joint inflammation is caused by the formation of monosodium urate monohydrate (MSU) crystals

within the joint space. Osteoarthritis is a degenerative cartilage disorder; cartilage breakdown causes bones to rub against each other. Causes include injuries, diseases such as Paget's disease, and long-term obesity, but often the cause is unknown. Complicating matters further is that fibromyalgia is sometimes also intended to be included in the loose term "arthritis". There is also Psoriatic Arthritis, one of the seronegative spondyloarthropathies, which is believed to be autoimmune in origin but is a separate disorder from Rheumatoid arthritis and whose exact cause is unknown, but there is a clear genetic component. Another of the seronegative spondyloarthropathies is Ankylosing spondylitis (also known as Bechterew syndrome; Marie Strumpell disease; and rheumatoid spondylitis). There is also an assortment of infectious arthritis, i.e. arthritis caused by bacteria, rickettsiae, mycoplasmas, viruses (or vaccinations given to prevent viral infections), fungi, or parasites. Included in this category are various types of septic arthritis, mycotic arthritis, and viral arthritis, such as rubella arthritis, Lyme arthritis, Mumps arthritis, arboviral arthritis, syphilitic arthritis, parvovirus arthritis, tuberculous arthritis, Varicella arthritis, gonococcal arthritis, rubella arthritis, Reiter's syndrome (which includes a form of arthritis commonly arising from infection by Chlamydia trachomatis) etc. These assorted disorders can arise from quite varied sources. Moreover, there is also a poorly understood disorder, pseudoseptic arthritis. In addition, CPDD (sometimes called pseudoosteoarthritis, or pseudogout) arises from Calcium Pyrophosphate Deposition. Systemic onset juvenile idiopathic arthritis (SOJIA, also known as Still's disease), unlike rheumatoid arthritis, appears dependent on IL-1 and dendritic cell malfunction, and has a substantial numbers of syptoms associated with it, including hepatosplenomegaly and vasculopathy. There is also Adult Still's disease (ASD or AOSD)

which has in addition to joint inflammation, a salmon-pink rash and daily spiking fevers. Menopausal arthritis is due to ovarian hormonal deficiency. Neuropathic arthritis (which comes in several forms, the most important of which is Charcot's disease) can arise from sources as diverse as Diabetes Mellitus, Steroid treatment, Leprosy, Chronic alcoholism, Heavy metal poisoning and Neoplastic peripheral neuropathy. There is also type II collagen-induced arthritis (CIA). ***Hallux rigidus*** is a degenerative type of arthritis that affects the large joint at the base of the big toe; why this degenerative process occurs is unknown. There is simply no way of knowing which one of these disorders applicants intend. For whichever choice is made, applicants must show that one of ordinary skill in the art would have known that this choice, and not another, was intended, and applicants must correct the term (paragraph 2).

Claim 8 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The word "optionally" needs to be removed; for a true composition, the carrier, etc. is not optional.

Claims 10, 16, 19-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for type-2 diabetes and obesity, does not reasonably provide enablement for type I diabetes, or arthritis.3 The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Pursuant to ***In re Wands***, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), one considers the following factors to determine whether undue experimentation is

required: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. Some experimentation is not fatal; the issue is whether the amount of experimentation is "undue"; see ***In re Vaeck***, 20 USPQ2d 1438, 1444.

The analysis is as follows:

(1) Breadth of claims. Owing primarily to the wide scope of the four primary variables, billions of compounds are covered. As noted above, "arthritis" covers a number of largely unrelated disorders.

(2) The nature of the invention and predictability in the art: The invention is directed toward medicine and is therefore physiological in nature. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See ***In re Fisher***, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

(3) Direction or Guidance: That provided is very limited. The dosage range information on apparently was omitted from the specification.

(4) State of the Prior Art: These compounds are xanthines with a particular substitution pattern at the 1, 3, 7- and 8-positions. So far as the examiner is aware, no xanthines of any kind have been used for the treatment of arthritis, or Type I diabetes, etc. Indeed, the examiner must note that these are purines, and those with gouty arthritis are specifically told to avoid foods rich in purines.

(5) Working Examples: There are none for the treatment of any disease. There is a test showing that these compounds are inhibitors of DPP-IV, but this is not a standard test for any of these utilities

(6) Skill of those in the art: No one medicine could possibly treat all of the diverse types of arthritis generally. They are simply too diverse. Thus, for example, Psoriatic Arthritis, CPDD, syphilitic arthritis and Osteoarthritis have utterly different etiology, and it would be contrary to medical science for one drug to be able to treat all four.
Rheumatoid arthritis is an inflammatory disorder causing destruction of articular cartilage, in which macrophages accumulate in the rheumatoid synovial membrane. Mediators are cytokines, including IL-1, IL-18, α-TNF and IFN-K. It is thus an autoimmune condition where the body's immune system attacks its joints. The skill level in treating Rheumatoid arthritis is relatively low. The main animal model, AIA, has not proved to be a reliable predictor of which compounds will actually prove effective in humans. There are only a very few compounds which treat RA per se, and these are all α-TNF inhibitors, not a property that these compounds are disclosed to have. Type I Diabetes treatment, what little there is, tends to be via immune suppressants, since this is an auto-immune disorder.
(7) The quantity of experimentation needed: Owing especially to factors 1, 4, 5 and 6, the amount of experimentation is expected to be high.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. ***In re Wright***, 999

F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here.

Claims 1-3, 8, 10, 12, and 16-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for other choices, does not reasonably provide enablement for R4 as XI-XIV and XXVII-XXX. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The process as presented in the specification will not prepare compounds with R4 groups bound via C. For example, if R4 is cyclohexyl substituted by amino, this reaction simply will not work. It will give the wrong product, i.e. amino substituted by cyclohexyl.

Claim Objections

Claims 4-6, 14 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to /Mark L. Berch/ whose telephone number is 571-272-0663. The examiner can normally be reached on M-F 7:15 - 3:45.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on (571)272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Mark L. Berch/
Primary Examiner
Art Unit 1624

4/21/2008